IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	**DC-0257**
Inventors:	**Buckey et al.**
Serial No.:	**10/786,429**
Filing Date:	**February 25, 2004**
Examiner:	**San Ming R. Hui**
Customer No.:	**26259**
Group Art Unit:	**1617**
Confirmation No.:	**1958**
Title:	**Methods of Preventing or Treating Motion Sickness**

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I hereby certify that this paper is being electronically submitted on the date indicated above to the Commissioner for Patents, U.S. Patent & Trademark Office (AF).

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Commissioner for Patents
U.S. Patent & Trademark Office
(AF)

REPLY BRIEF

This is in response to the Examiner's Answer dated November 26, 2008, which raised certain issues that Appellants wish to address.

Regarding the Examiner's rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (1988), in view of Drug Information Handbook, the British Medical Journal (1970), Weinstein et al. (1997), and Kohl et al. (1991), the Examiner states that the "alleged 2-order of magnitude of dosage by Appellant is incorrect" (see page 5, first paragraph of the Examiner's Answer). However, Appellant respectfully points out that the Examiner has apparently not understood that the Appellants assertions regarding the 2-order of magnitude difference in dosage refer to differences in doses as they would be corrected to apply to humans. The Examiner is correct in stating that the 20 mg/kg subcutaneous dose in a shrew (the test species of Ueno et al.) is indeed in the range of 1 mg when corrected for the body weight of the shrew. However, in the rejection under 35 U.S.C. 103(a), the Examiner is applying this paper to make obvious dosing in humans. As Appellants explained in the Appeal Brief (see pagers 8 and 9), the dose claimed in pending claim 1 is a 12 mg human dose. As such, that dose in humans would equate to 0.2 mg/kg in humans, when the dose is converted to a mg/kg dose basis. Now, when that dose is compared to the dose taught in Ueno et al. (20 mg/kg), that dose is 2 orders of magnitude larger than the dose that is recited in claim 1 of the instant case. Nowhere have Appellants suggested that one should extrapolate from a subcutaneous dose in a shrew to an oral dose in humans. As such, the Examiner's statements regarding extrapolation of the dose in shrews are incorrect. Evan if one of skill were to extrapolate from the dose taught

for use in shrews, one would extrapolate to humans based on mg/kg, not mg doses. As a result, the reference of Ueno et al. (1988) teach one of skill that use of a dose of 20 mg x 70 kg average human body weight, or 1400 mg is appropriate and would be dose expected to have pharmacological activity in a human.

Moreover, Appellants respectfully disagree with the Examiner's statements regarding route of administration on pages 5 and 6 of the Examiner's Answer. Although chlorpheniramine may be active both orally and subcutaneously, it is not appropriate to extrapolate from the dose subcutaneously, as in Ueno et al. (1988), to a dose orally, as claimed. Teaching of a dose given by an entirely different route of administration (subcutaneously by Ueno et al. versus orally as claimed) does not provide one of skill with en expectation of success of using a drug effectively by another route. As explained out in the Appeal Brief at pages 9-10, it is a general principle of pharmacology that efficacy of a drug is effected by the route of administration. Thus, in the case of the instant invention, where the Examiner has suggested that data from subcutaneous administration of a drug predict what one of skill would expect to see with an entirely different route, is not correct. In the specification as filed, the data provided to enable the claimed invention is based on administration of chlorpheniramine orally to humans. In the study by Ueno et al. (1988) cited by the Examiner, chlorpheniramine was shown to have anti-nausea effects when administered subcutaneously at a much higher dose, not orally. It is also a general principle of pharmacokinetics (the scientific discipline that studies how a drug arrives at its site of action to produce its effects, and how a route of administration affects the required effective dose of a drug)

that a drug administered subcutaneously would have a different dose-response relationship for efficacy than that same drug would have if administered orally. Therefore, contrary to the Examiner's suggestion, one of skill would not use data on subcutaneous administration of a much higher dose of a drug to predict a dose level that would be effective orally for the same drug at a much lower dose.

As a result, the burden of establishing that the cited documents make obvious the present invention under 35 U.S.C. 103(a) has not been met by the Examiner. Therefore, this rejection cannot be upheld.

Respectfully submitted,

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